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(11) Sand, "Experimenteller Hermaphroditismus," 'Pflügers Arch.,' vol. 173 (1919); 'Experim. Studier over Kønskarakterer hos Pattedyr.,' Copenhagen, 1918; "Experiments on the Internal Secretion of the Sexual Glands," 'Jl. of Physiol.,' vol. 53 (1919).

The Influence of Various Conditions on the Time Relations of Tendon Reflexes in the Human Subject.

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The following observations constitute a preliminary account of an investigation into the time relations of certain reflexes in the human subject. The knee-jerk was primarily selected for study. The variability of magnitude of the knee-jerk in response to equal stimuli has been commented on by the majority of observers, and, according to Scheven,* such a variable response may occur even in the decerebrate animal. Whether variations of the irritability of the spinal reflex centre take place in the intact human subject there is no means of knowing, but study of the human responses has convinced us that by far the greatest factor in determining the variability of the knee-jerk is cortical activivity, and that, by taking suitable precautions, variability may be reduced to a negligible factor. In a previous publication, one of us (F. G.)* has shown that these variations of the knee-jerk are secondary to alterations in the tonus of the quadriceps muscle. It was found that any stimulus of a nocuous nature, whether physical or psychical, caused an increase in the quadriceps tonus when the limb was flexed in the position in which the knee-jerk is elicitable, and that the magnitude of the knee-jerk was correspondingly increased. Similarly, pleasurable stimuli leading to an inhibition of effort were responded to by diminished quadriceps tonus and a diminished knee-jerk.

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* Scheven, 'Pflüger's Arch. f. d. ges. Physiologie,' vol. 117, p. 108 (1907).

It was found in our present experiments that, by using a trained subject and avoidance of all sources of psychical disturbance, it was possible to obtain responses to uniform stimuli which only rarely showed any irregularity. Neglect of the psychical factor has been the cause of the irregularity of response noted by so many observers. Uniformity of the stimulus was secured by the use of electrically released pendulums, which could be weighted to any desired extent. The relatively inefficient slow pushing stroke of the pendulum on the patellar tendon was converted into a more efficient stimulus of briefer duration by interposing a small piece of metal-covered wood, held in position by a stout springy steel rod. This anvil, for the reception and conversion of the pendulum blow, is adjusted in contact with the patellar tendon, and on the pendulum striking it the circuit of a Deprez signal is closed, and the moment of stimulation is photographed on the recording paper. The muscular response was recorded by photographing the excursions of the string of an Einthoven galvanometer, through which the muscle current of the quadriceps was led. For observation of more than one group of muscles simultaneously, a galvanometer with two strings was employed, and the muscle currents were explored by fine needle electrodes pushed into the substance of the muscle.

The Influence on the Latent Period of Conditions affecting the Magnitude of the Knee-jerk.—The magnitude of the response shows a direct relation to the strength of the stimulus, and, as already noted by Hoffmann,† there is a diminution of the latent period when the response is increased by a larger stimulus. We were able to confirm the observation of Dodge,‡ that the diminution of the latent period has a direct relation to the strength of the stimulus. Progressively weighted pendulums were used, the velocity of the pendulum remaining constant. The maximum diminution of the latent period obtained by using as large a stimulus as could be conveniently borne was 2·6 sigma. That this diminution is not due to a larger muscle current accelerating the movement of the galvanometer string was shown by records taken of the latent period of the electromyogram when the motor nerve was stimulated electrically, so as to give small maximal responses. As the quadriceps is unsuitable for this experiment, the determinations were made on the supinator longus muscle, the nerve being stimulated at the bicipital groove. With the galvanometer string at the same degree of tension as in the knee-jerk experiments, it was found that there was no measurable shortening of the latent period when minimal and maximal stimuli were recorded. The shortening of the latent period must, therefore, be referred either to the receptor portion of the reflex arc or to the central "synapse" time. Further observations when the increased response is due to central causes tend to show that the synapse time may be increased or diminished. The increased knee-jerk during either physical or psychical effort is accompanied by a diminution of the latent period. This was denied by Hoffmann, but in a series of thirty-five experiments we never failed to obtain this result. A large number of measurements showed that the diminution of the latent period was proportional to the increase of the muscular response. The decrease of the latent period and the increase in the magnitude of the knee-jerk showed a rough correspondence to subjective estimates of the degree of intellectual or physical effort exerted or to the intensity of the nocuous stimulus applied. The shortening of the latent period was found to be as much as 4·2 sigma when a maximal physical effort was made, and the knee-jerk record compared with that obtained when the body and mind were in repose. It is very improbable that this reduction of the latent period can be referred to any facilitation of stimulation by the increased tonus of the quadriceps, since the maximal reduction of latent time is twice as great as can be effected by changing from a small to a large stimulus. It appears to us to be reasonable to impute it to a reduction of the central or "synapse" time.

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* Golla, "Croonian Lectures," 'Lancet,' 1921.

† Hoffmann, 'Archiv f. Anat. u. Physiologie,' p. 223 (1910).

‡ Dodge, 'Zeitschrift für Allg. Physiologie,' vol. 12 (1911).

The Influence of Various Conditions on the Refractory Period of the Knee-jerk.—By using a pair of similar pendulums, so arranged that one can be released at any desired period after the other, the refractory period of the reflex can be estimated.

When a stimulus of an energy value of 1638 grm.-cm. was used, it was noted that when the second stimulus fell 280 sigma after the first, there was a slight diminution in the magnitude of the second response. This diminution progressed as the second stimulus was approached nearer and nearer to the first, the curve of the diminution of the second response being of a logarithmic type reminiscent of a fatigue curve till, when the interval between the two stimuli was 200 sigma, the second response disappeared completely. The onset of the relative refractory period and the time interval at which it becomes total are influenced by conditions determining the effectiveness of the stimulus. When an absolute refractory state has been established to a second stimulus an increase in the strength of the stimulus will break down the refractory state. Similarly, physical or psychical effort sufficient to cause an increase in the quadriceps tone will break down a refractory state, providing that the second stimulus be delivered at the extreme limit of the refractory state. When the second stimulus is brought still nearer to the first, it becomes increasingly difficult to break down the refractory state.

A study of the time relations of the onset of total refractory states to the strength of the stimulus affords compelling evidence that the knee-jerk, in so far as each participating neurone is concerned, is an "all-or-none" reflex. The grading of the reflex response being due to the participation of a greater number of neurones when the stimulus is increased. This conclusion appears to be warranted by the fact that the duration of the refractory period is independent of the strength of the first stimulus. Thus with two successive equal stimuli of an energy value of 1638 grm.-cm. each, the reflex was absolutely refractory to the second stimulus when this approached to 200 sigma. When the energy value of the first stimulus was increased six-fold to 9045 grm.-cm., whilst the second stimulus remained unchanged the refractory period was unaffected. When with the first stimulus at 1638 grm.-cm., the second stimulus was increased to 9045 grm.-cm., the refractory period became absolute when the second stimulus was within 140 sigma of the first. When both stimuli were increased to 9045 grm.-cm. each, the refractory period remained shortened at 140 sigma. We consider that these results offer evidence in favour of the all-or-none hypothesis.

Although the refractory period is relatively long when tested by a single pair of stimuli, it undergoes a marked diminution when the patellar tendon is subjected to a series of rapid stimuli. To effect this a tapping machine, driven by an electro-motor, was designed to deliver any desired number of stimuli in a second, the stimuli being signalled in the usual fashon. A single pair of stimuli from this machine yielded the same refractory period as was obtained with a pair of pendulums. When, however, a series of stimuli, each at a shorter interval than had been ascertained to be that of the refractory period, was administered, after the first four or five stimuli the knee jerk began to respond to each individual stimulus, the rate of tapping could be increased with each stimulus, eliciting an effective response up to twenty taps per second. *Pari passu* with the increase of the rapidity of the tapping, the magnitude of the individual responses diminished till, at a little above the frequency of twenty per second, they become unreadable. This diminution in the magnitude of the response is of a different order to the diminution obtained in the response to the second stimulus, when experimenting with a pair of stimuli at decreasing intervals. With the isolated pairs of stimuli the second response would begin to diminish at an interval of about 250 sigma between the stimuli, and would entirely disappear when the interval was 200 sigma, whereas with multiple tapping, the responses began to diminish when the interval between stimuli was about 200 sigma and disappeared altogether when the interval was reduced to 50 sigma. Unlike the curve of diminution of the second response when pairs of stimuli at diminishing intervals are studied, the responses with increased rate of tapping diminished in a straight line, and this diminution was probably the expression of the increased inefficiency of the stimulus delivered at very short intervals on the yielding patellar tendon before it has time to recover.

A measurement of the latent period of the responses when the stimuli are administered at the rate of twenty per second showed that the latent period was about 13 sigma. The diminution of the latent period from that of a single stimulus administered with the same machine was about 7 sigma. If Hoffmann's calculation founded on Eulenburg's measurements of the length of the reflex arc be accepted allowing 0·0077 seconds for nerve conduction and 0·0036 seconds for the latent period of the muscle, the "synapse time" is 9 sigma. Such calculations are necessarily only approximate, since *inter alia* we are unaware of the seat of the receptors of the stimulus of the knee-jerk which may be in the patellar tendon or as Hoffmann supposes in the belly of the muscle, and further no allowance is made for the latent time of the receptors. It seems, however, to be fairly certain that accepting Piper's figure for the velocity of conduction of a nerve impulse, which we have independently confirmed, a latent period of less than 13 sigma for the reflex in a man of normal height would leave less than 1½ sigma available for synapse time. It would appear then that when the knee-jerk is elicited by such a high rate of stimuli as twenty per second, synaptic delay may cease and the reflex arc functions as a nerve muscle preparation. The mechanical difficulties that render taps on the patellar tendon at a greater rate than that of twenty per second inefficient would appear to be the only obstacle to obtaining responses at a far higher rate.

The time relations of the response of the flexors of the knee in the knee jerk were next determined. The stimulus was signalled as usual. One string of the Einthoven galvanometer was connected with the electrodes applied to the quadriceps, and the other string was connected to needle electrodes plunged into the flexor muscles. It was found that, in the patellar reflex, the flexor group contracted with a simple twitch 7 sigma later than the quadriceps.

A similar experiment was made with the ankle jerk. Here it was found that, as in the knee jerk, the antagonist group contracts, the anterior tibials contracting 10 sigma later than the gastrocnemius. In both cases, it is obvious that this contraction of the antagonist muscles cannot be a secondary reflex in response to the joint movement, on account of the very short period separating it from the contraction of the prime movers. Neither is the contraction a purely muscular response to a sudden stretch of the tendon from the reflex movement, since it occurs when the joint is immobilised. It would appear, therefore, that in each case the contraction of the prime movers, and subsequently of the antagonists, constitutes a prearranged reflex pattern in the cord which is discharged by the appropriate tendon stimulation. If this view be correct, it might be anticipated that the reflex pattern would also appear when the reflex movement was imitated by a voluntary movement of similar scope. This proves to be the case. A rapid voluntary extension of the knee in imitation of the knee jerk gave rise to a primary contraction of the quadriceps, followed, after an interval of 10 sigma, by a contraction of the flexors. The records only differing from those obtained with the patellar reflex in that, instead of a single twitch, both muscle responded by a number of diphasic oscillations at the rate of about 50 per second. Precisely similar results were obtained on imitating the ankle jerk by a voluntary pointing of the toes, the anterior tibials entering into the characteristic voluntary 50 per second discharge 10 sigma later than the gastrocnemius.

Conclusions.—The latent period of the knee-jerk varies inversely with the magnitude of the response, whether the magnitude be influenced by the strength of the stimulus or by the effect of physical or psychical effort, with a corresponding increase of the quadriceps tonus. These diminutions of the latent period appear to be at the expense of the synapse time.

The synapse delay may be very greatly reduced, if not abolished, when the knee-jerk is elicited by rapidly repeated stimuli.

The refractory period of the knee-jerk is not absolute, but is relative to the strength of the stimuli used in its determination. It can be very much diminished by a sufficiently rapid stimulation of the tendon. The duration of the refractory period bears no relation to the strength of the initial stimulus.

The knee-jerk would, therefore, appear to be an "all-or-none" response for each single neurone concerned in it.

The antagonistic muscles in the knee-jerk—the flexor group—and in the ankle-jerk—the anterior tibial group—enter into contraction about 10 sigma after the beginning of the response of the quadriceps and the gastrocnemius respectively.

This contraction of the antagonists forms part of the spinal reflex pattern elicited by the tendon stimulation, and such a reflex pattern is made use of in voluntary movements of a like nature to the reflex movement.

In conclusion we wish to express our thanks to Sir Frederick Mott for the facilities that he afforded us for carrying out these experiments in his laboratory at the Maudsley Hospital. We are, in addition, deeply indebted to him for much valuable advice.

An Abnormal Relationship of the Electrical to the Mechanical Response in the Ventricles.

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[Plate 1.]

The record described in this paper was made on a man aged 64, who was suffering from complete heart block (Plate 1, fig. 1). The characteristic features peculiar to it were observed on one occasion only, although numerous other records were made on the same subject. It was impossible to continue the observations as the patient developed acute tonsillitis and died of œdema of the glottis.

The observation in question is shown in Plate 1, fig. 2, in which the lower record is an electrocardiogram taken with a sensitive string at about one-eighth of the usual magnification, and the upper record is a combined carotid and radial sphygmogram taken by a method previously described by Bramwell and Hill (5), employing a hot-wire sphygmograph (1) (2). In this particular instance the carotid receiver was placed low down in the neck, and consequently not only arterial but also certain additional waves from the internal jugular vein were recorded.

The spacing of the ventricular complexes of the three electro-cardiograms differs from that of the three arteriograms. For purposes of comparison it is convenient to select similar points in the three cycles; and those which present the greatest facility for accurate measurement, in this record, are the